



# Comparing the Effect of Granisetron with Meperidine on Post-Shivering in Elective Cesarean Section under Spinal Anesthesia

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## Abstract

**Background:** Post-operative shivering after spinal anesthesia is a common issue in women undergoing cesarean section, then its management is necessary to increase patients' satisfaction. Therefore, the current study aimed to compare the prophylactic effect of Granisetron and meperidine on post-spinal shivering in elective cesarean section.

**Methods:** In this double-blinded clinical trial study, 100 women under elective cesarean section using block randomization were divided into two groups. The spinal anesthesia was performed in all women with 10 mg hyperbaric bupivacaine 0.5 %. Then, after the birth of the baby, the patients received 0.04 mg/kg Granisetron or 0.4 mg/kg meperidine intravenously. Mean Arterial Pressure (MAP), Heart Rate (HR), and percentage of arterial blood oxygen saturation (SpO<sub>2</sub>) were measured before intervention and 60 minutes after surgery using a standard monitoring device. Shivering was evaluated 30 minutes after the surgery in the recovery room according to the clinical examinations.

**Results:** The changes in hemodynamics parameters were similar between the two groups. There was a statistically significant difference in the rate of shivering between the two groups. The rate of shivering in the Granisetron group was higher than in the meperidine group. Thus, 13 patients (26%) and 5 patients (10%) had shivering in the Granisetron and meperidine groups, respectively (p=0.037).

**Conclusion:** Granisetron was not more effective than meperidine as routine treatment in preventing shivering after spinal anesthesia in women under elective cesarean section.

**Keywords:** Cesarean section, Granisetron, Meperidine, Shivering, Spinal anesthesia

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**Received:** Jul 19 2023

**Accepted:** Nov 6 2023

## Citation to this article:

Karami T, Hooshyar H, Hanari H. Comparing the Effect of Granisetron with Meperidine on Post-Shivering in Elective Cesarean Section under Spinal Anesthesia. *J Iran Med Council.* 2024;7(4):725-30.

## Introduction

Spinal Anesthesia (SA) is commonly used in patients undergoing Cesarean Section (CS) (1). Post-operative shivering after spinal anesthesia is a common problem in patients undergoing CS and its incidence was reported as 50-55% up to 80% in previous studies (2,3). Hypothermia and shivering may have different complications such as surgical site infection, myocardial ischemia, and perioperative coagulopathy (4). Shivering may increase oxygen consumption which will impact negatively heart rate, oxygen saturation, and blood pressure (5,6).

Shivering is defined as a spontaneous and involuntary rhythmic oscillatory contraction of muscles (7). The etiology of shivering is not clear yet and it may be multiple mechanisms (1,8). Various causes for shivering after surgery have been stated, including spinal reflexes, decreased sympathetic activity, suppression of the adrenal gland, and respiratory alkalosis (2).

To prevent the post-operative shivering in patients undergoing CS, several drugs have been used including meperidine, Granisetron, ketorolac, ondansetron, nalbuphine, ketamine, tramadol, and dexmedetomidine (5,9-15). The effect of meperidine or Granisetron on post-operative shivering after spinal anesthesia in CS alone compared to other drugs has been investigated in previous studies (9,11,16,17). To the best of our knowledge, only in a study, the prophylactic effect of Granisetron and meperidine on post-spinal shivering has been evaluated and its results demonstrated that Granisetron was effective compared to meperidine in reducing post-spinal shivering in patients undergoing CS (12).

Yet, shivering is the most common problem in cesarean delivery following spinal anesthesia, then its management was necessary for increasing patient satisfaction. Therefore, to find the ideal drug that has a better effect on reducing shivering and lack of enough studies, the current study aimed to compare the prophylactic effect of Granisetron and meperidine on post-spinal shivering in elective CS.

## Materials and Methods

In this double-blinded clinical trial, 100 women of 20 to 40 years with ASA II status undergoing spinal anesthesia for elective cesarean section were

enrolled. Women with chronic diseases including hypertension, diabetes, psychological disorders, parturient presenting with shivering before delivery, temperatures greater than 38°C or less than 36°C, and surgeries longer than an hour were excluded.

The study was a double-blind clinical trial. The patients and researcher who evaluated the outcomes were blind about the allocation of the patients into Granisetron or meperidine groups. The anesthesiologist that prescribed the drugs was other than the outcome assessor. The patients were divided into two groups using block randomization based on generated-numbers by random allocation software. Thus, the table of computer-generated numbers was given to the anesthesiologist, who entered the patients into groups according to the order of numbers. Finally, the groups' names were encoded with the letters A and B.

The temperature of the operating room was kept instantly using a calibrated temperature in two groups. The spinal anesthesia was performed in all the patients using a standard 25 Quincke needle at L3-4 with 10 mg hyperbaric bupivacaine 0.5%. During the anesthesia, oxygen was given, and the patients were covered. All the fluids were warmed to 37°C. The temperature of the operating and recovery room was the same between 23-25°C for all the patients. Also, both groups received 3 ml of Ringer's serum at room temperature. Then, after the birth of the baby, the patients received 0.04 mg/kg Granisetron (Granisetron group) or 0.4 mg/kg meperidine (meperidine group) intravenously. In cases with HR < 50 0.5 mg atropine and decreasing over 20% of Mean Arterial Pressure (MAP) 5 mg of ephedrine was injected and if more atropine or ephedrine was used, the patient was excluded from the study. In patients who experienced shivering after the surgery, 30 mg of meperidine was injected to treat it.

MAP, Heart Rate (HR), and percentage of arterial blood oxygen saturation (SpO<sub>2</sub>) were measured before intervention and 60 minutes after surgery using a standard monitoring device. Shivering was evaluated 30 minutes after surgery in the recovery room according to clinical examination. Shivering was evaluated as 0: Non-shivering; 1: Piloerection or peripheral vasoconstriction, but no visible shivering; 2: Muscular activity only in one muscle group; 3:

Muscular activity in more than one muscle group, and 4: Shivering involving the whole body. The temperature of the recovery room was kept instantly using a calibrated temperature in the two groups.

### Statistical Analysis

The data were presented as mean±standard deviation (SD) or number (percentage) for continuous or categorical variables, respectively. The normality of the data was tested using the Kolmogorov-Smirnov test. A paired T-test was utilized to compare the mean of MAP, HR, and SpO<sub>2</sub> within the groups. The mean of variables at baseline and after the intervention was compared using an Independent T-test between the two groups. The chi-square test was used to compare the shivering frequency between the two groups. Data analysis was performed by SPSS17 (IBM Corp., Armonk, New York, USA) and p-values less than 0.05 were considered statistically significant.

### Results

In this study, 100 women (50 women in each group) were analyzed. The demographic characteristics were not statistically significant between the two groups ( $p>0.05$ ). All the patients had ASA II in both groups and the mean age was close in the two groups (data

are not shown).

The hemodynamic parameters were not statistically significant between the two groups at baseline (p-values for MAP=0.784, HR=0.597 and, SpO<sub>2</sub>=0.75). The changes in SpO<sub>2</sub> were similar in both groups. As in the Granisetron group, SpO<sub>2</sub> increased significantly from 97.66±1.23 at baseline to 99.26±1.06 after the intervention and from 97.1±1.51 at baseline to 99.3±1.11 after the intervention in the meperidine group ( $p=0.001$ ). In the Granisetron group, MAP and HR had no significant changes compared to the baseline. In the meperidine group, MAP had no significant changes compared to the baseline; but the HR decreased significantly from 98.18±13.21 at baseline to 92.82±14.54 after intervention ( $p=0.024$ ). There was no statistically significant difference in any of the hemodynamic parameters after the intervention between the two groups ( $p>0.05$ ) (Table 1).

There was a statistically significant difference in the rate of shivering between the two groups. The frequency of shivering in the Granisetron group was higher than the meperidine group in the recovery room among women under elective cesarean section. Therefore, 13 women (26%) and 5 women (10%) had shivered in the Granisetron and meperidine groups, respectively ( $p=0.037$ ) (Table 2).

**Table 1.** Comparison of hemodynamic parameters at baseline and after intervention between groups

Hemodynamic variables	Granisetron group (n=50)			Meperidine group (n=50)				
	Before	After	P1	Before	After	P1	P2	P3
MAP	101.30±11.5	98.02±12.92	0.797	101.96±12.43	98.8±12.34	0.866	0.784	0.758
HR	96.84±12.05	94.8±11.84	0.343	98.18±13.21	92.82±14.54	0.024	0.597	0.457
SpO <sub>2</sub>	97.66±1.23	99.26±1.06	0.001	97.1±1.51	99.3±1.11	0.001	0.75	0.85

P1: Within -group comparison using Paired t-test

P2: Mean comparison before the intervention using an independent t-test between two groups.

P3: Mean comparison after the intervention using an independent t-test between two groups.

**Table 2.** Comparison of shivering frequency at recovery between groups

	Granisetron group, n(%)	Meperidine group, n(%)	p-value
Shivering	No	37(74)	0.037
	Yes	13(26)	

## Discussion

Shivering is usually triggered by hypothermia, but it may occur in patients with a normal temperature in the postoperative during spinal anesthesia (6). The incidence of shivering has been reported up to 80% in patients undergoing cesarean delivery following spinal anesthesia (3).

Nowadays, spinal anesthesia in obstetric surgery, especially cesarean section is common. The complications of spinal anesthesia such as shivering are more common in patients undergoing cesarean delivery, and finding a better drug to prevent shivering is necessary (1). Hence, the current study aimed to compare the prophylactic effect of Granisetron and meperidine on post-spinal shivering in elective cesarean section.

In the present study, it was shown that the incidence of shivering in the Granisetron group (26%) was significantly higher than in the meperidine group (13%) during recovery among women under elective cesarean section.

The effect of meperidine on shivering in elective cesarean section has been investigated in the previous study (16-19). Some studies demonstrated that meperidine may be effective in reducing the rate of post-spinal shivering cesarean delivery, but its use may be associated with an increased incidence of nausea and vomiting (18,19). A study by Tilahun *et al* revealed that the effect of tramadol and meperidine on controlling shivering was similar in women undergoing cesarean section under spinal anesthesia, but tramadol has fewer side effects compared to meperidine (16). Also, Mahoori *et al*'s study suggested that ondansetron and meperidine have similar effects on shivering after general anesthesia (20). Another study indicated that low-dose tramadol (0.5 mg/kg) is superior to meperidine, and fentanyl (17). A study by Roy *et al* demonstrated that intrathecal meperidine (0.2 mg/kg) is effective in reducing shivering after spinal anesthesia in cesarean delivery (18).

Meperidine prevents shivering by affecting the central nervous system and increasing the shivering threshold. Also, serotonin agonist drugs such as Granisetron increase body temperature and prevent shivering by preventing the uptake of 5-hydroxytryptamine in the preoptic area of the hypothalamus (6).

Some previous studies showed that Granisetron

effectively reduced the incidence of shivering compared to placebo and meperidine in the cesarean section under spinal anesthesia (13,19-21), while in other studies, no significant difference was observed between Granisetron and other drugs used to control shivering (9,11,22).

The current study suggested that meperidine was more effective than Granisetron in preventing shivering and on the other hand, the effects of these drugs on hemodynamic parameters were similar. In contrast to our findings, a study showed that Granisetron 0.4 mg/kg was more effective than meperidine 0.4 mg/kg and both of them were more effective compared to hydrocortisone 2 mg/kg in reducing shivering during spinal anesthesia (12).

In the present study, shivering intensity, nausea and vomiting have not been evaluated. According to studies, Granisetron is effective in preventing nausea and vomiting through the inhibition of serotonin receptors, and it is better to use Granisetron instead of meperidine in cases of shivering with nausea and vomiting.

## Conclusion

Granisetron was not more effective than meperidine as routine treatment in preventing shivering after spinal anesthesia in women under elective cesarean section. Further studies with controlling all possible confounders are recommended.

## Acknowledgement

The authors appreciate statistical counselors of the Clinical Research Development Unit of Imam Khomeini Hospital, Urmia University of Medical Sciences. This study was approved by the Ethics Committee of Urmia University of Medical Sciences (ID: IR.UMSU.REC.1401.002), and it has been registered in the Iranian Registry of Clinical Trials (IRCT) with ID: IRCT20170516033992N10.

## Conflict of Interest

There was no conflict of interest in this manuscript.

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